Antepartum Care (Updated September 14, 2011)

General Principles Regarding Use of Antiretroviral Drugs During Pregnancy

Panel's Recommendations
• Initial evaluation of infected pregnant women should include assessment of HIV disease status and recommendations regarding initiation of antiretroviral (ARV) drugs or the need for any modification if currently receiving antiretroviral therapy (ART) **(AIII)**. The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.
• Regardless of plasma HIV RNA copy number or CD4 cell count, all pregnant HIV-infected women should receive a combination antepartum ARV drug regimen to prevent perinatal transmission **(AI)**. A combination regimen is recommended both for women who require therapy for their own health **(AI)** and for prevention of perinatal transmission in those who do not yet require therapy **(AII)**.
• The known benefits and potential risks of ARV use during pregnancy should be discussed with all women **(AIII)**.
• ARV drug-resistance studies should be performed before starting or modifying ARV drug regimens in women whose HIV RNA levels are above the threshold for resistance testing (e.g., >500 to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AI)**. When HIV is diagnosed late in pregnancy, ARV therapy or prophylaxis should be initiated pending results of resistance testing **(BIII)**.
• In counseling patients, the importance of adherence to the ARV regimen should be emphasized **(AII)**.
• Considerations regarding continuation of the ARV regimen for maternal therapeutic indications after delivery are the same as for nonpregnant individuals. The pros and cons of continuing versus discontinuing ARV drugs postpartum should be discussed with women so they can make educated decisions about postpartum ARV use before delivery **(AIII)**. Such decisions should be made in consultation with the provider who will assume responsibility for the women's HIV care going forward after delivery.
• Coordination of services among prenatal care providers, primary care and HIV specialty care providers, mental health and drug abuse treatment services, and public assistance programs is essential to ensure that infected women adhere to their ARV drug regimens **(AIII)**.

In addition to the standard antenatal assessments for all pregnant women, the initial evaluation of an HIV-infected pregnant woman should include an assessment of HIV disease status and recommendations for HIV-related medical care. This initial assessment should include the following:

a. review of prior HIV-related illnesses and past CD4 cell counts and plasma HIV viral loads;

b. current CD4 cell count;

c. current plasma HIV RNA copy number;

d. assessment of the need for prophylaxis against opportunistic infections (OIs) such as *Pneumocystis jirovecii* pneumonia (PCP) or Mycobacterium avium complex (MAC) (see Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents)[1];

e. evaluation of immunization status per guidelines from the American College of Obstetricians and Gynecologists, with particular attention to hepatitis A, hepatitis B, influenza, and pneumococcus immunizations[2];

f. baseline complete blood cell count (CBC) and renal and liver function testing;

g. HLA-B*5701 testing, if abacavir use is anticipated (see Table 5);

h history of prior and current ARV drug use, including prior ARV use for prevention of perinatal transmission of HIV or for treatment of HIV disease, and history of adherence problems;

i. results of prior and current HIV ARV drug-resistance studies; and

j. assessment of supportive care needs.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 1 of 11)

(See also Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy supplement for additional toxicity data and Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents for detailed guidelines regarding treatment options.)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
NRTIs			NRTIs are recommended for use as part of combination regimens, usually including two NRTIs with either an NNRTI or one or more PIs. Use of single or dual NRTIs alone is not recommended for treatment of HIV infection.		See text for discussion of potential maternal and infant mitochondrial toxicity.
Preferred Agents					
Lamivudine (3TC) Epivir	**Epivir** 150-, 300-mg tablets or 10-mg/mL oral solution **Combivir** 3TC 150 mg + ZDV 300 mg **Epzicom** 3TC 300 mg + ABC 600 mg **Trizivir**‡ 3TC 150 mg + ZDV 300 mg + ABC 300 mg	**Epivir** 150 mg BID or 300 mg once daily Take without regard to meals. **Combivir** 1 tablet BID **Epzicom** 1 tablet once daily **Trizivir** 1 tablet BID	Because of extensive experience with 3TC in pregnancy in combination with ZDV, 3TC plus ZDV is the recommended dual-NRTI backbone for pregnant women.	PK not significantly altered in pregnancy; no change in dose indicated[3]. High placental transfer to fetus.	No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects)[4]. Well-tolerated, short-term safety demonstrated for mothers and infants. If hepatitis B coinfected, possible hepatitis B flare if drug stopped postpartum, see Special Considerations: Hepatitis B Virus Coinfection.
Zidovudine (AZT, ZDV) Retrovir	**Retrovir** 100-mg capsules, 300-mg tablets, 10-mg/mL IV solution, 10-mg/mL oral solution **Combivir** ZDV 300 mg + 3TC 150 mg **Trizivir**‡ ZDV 300 mg + 3TC 150 mg + ABC 300 mg	**Retrovir** 300 mg BID or 200 mg TID Take without regard to meals. **Combivir** 1 tablet BID **Trizivir** 1 tablet BID	Preferred NRTI for use in combination ARV regimens in pregnancy based on efficacy studies and extensive experience; should be included in the antenatal ARV regimen unless there is severe toxicity, d4T use, documented resistance, or the woman is already on a fully suppressive regimen.	PK not significantly altered in pregnancy; no change in dose indicated[5]. High placental transfer to fetus.	No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects)[4]. Well-tolerated, short-term safety demonstrated for mothers and infants.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 2 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Alternative Agents					
Abacavir (ABC) Ziagen	**Ziagen** 300-mg tablets or 20-mg/mL oral solution **Epzicom** ABC 600 mg + 3TC 300 mg **Trizivir**‡ ABC 300 mg + ZDV 300 mg + 3TC 150 mg	**Ziagen** 300 mg BID or 600 mg once daily Take without regard to meals. **Epzicom** 1 tablet once daily **Trizivir** 1 tablet BID	Alternative NRTI for dual-NRTI backbone of combination regimens. See footnote regarding use in triple-NRTI regimen.‡	PKs not significantly altered in pregnancy; no change in dose indicated[6]. High placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. Hypersensitivity reactions occur in ~5%–8% of nonpregnant persons; a much smaller percentage are fatal and are usually associated with rechallenge. Rate in pregnancy unknown. Testing for HLA-B*5701 identifies patients at risk of reactions[7-8] and should be done and documented as negative before starting ABC. Patients should be educated regarding symptoms of hypersensitivity reaction.
Didanosine (ddI) Videx EC, generic didanosine enteric coated (EC) (dose same as Videx EC)	**Videx EC** 125-, 200-, 250-, 400-mg capsules Buffered tablets (non-EC) no longer available **Videx** 10-mg/mL oral solution	**Body weight ≥60kg:** 400 mg once daily; with TDF, 250 mg once daily **Body weight <60kg**: 250 mg once daily; with TDF, 200 mg once daily Take 1/2 hour before or 2 hours after a meal Preferred dosing with oral solution is BID (total daily dose divided into 2 doses)	Alternative NRTI for dual-NRTI backbone of combination regimens. ddI should not be used with d4T.	PKs not significantly altered in pregnancy; no change in dose indicated[9]. Moderate placental transfer to fetus.	Lactic acidosis, sometimes fatal, has been reported in pregnant women receiving ddI and d4T together[10-11].

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 3 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Emtricitabine (FTC) Emtriva	**Emtriva** 200-mg hard gelatin capsule or 10-mg/mL oral solution **Truvada** FTC 200 mg + TDF 300 mg **Atripla** FTC 200 mg + EFV§ 600 mg + TDF 300 mg	**Emtriva** 200-mg capsule once daily or 240 mg (24 mL) oral solution once daily Take without regard to meals. **Truvada** 1 tablet once daily **Atripla** 1 tablet at or before bedtime. Take on an empty stomach to reduce side effects.	Alternative NRTI for dual-NRTI backbone of combination regimens.	PK study shows slightly lower levels in third trimester, compared with postpartum[12]. No clear need to increase dose. High placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. If hepatitis B coinfected, possible hepatitis B flare if drug stopped postpartum, see Special Considerations: Hepatitis B Coinfection.
Stavudine (d4T) Zerit	**Zerit** 15-, 20-, 30-, 40-mg capsules or 1-mg/mL oral solution	**Body weight ≥60 kg:** 40 mg BID **Body weight <60 kg:** 30 mg BID Take without regard to meals. WHO recommends 30-mg BID dosing regardless of body weight.	Alternate NRTI for dual-NRTI backbone of combination regimens. d4T should not be used with ddI or ZDV.	PKs not significantly altered in pregnancy; no change in dose indicated[13]. High placental transfer.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. Lactic acidosis, sometimes fatal, has been reported in pregnant women receiving ddI and d4T together[10-11].

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 4 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Tenofovir Disoproxil Fumarate (TDF) Viread	**Viread** 300-mg tablet **Truvada** TDF 300 mg + FTC 200 mg **Atripla** TDF 300 mg + EFV§ 600 mg + + FTC 200 mg	**Viread** 1 tablet once daily Take without regard to meals. **Truvada** 1 tablet once daily **Atripla** 1 tablet at or before bedtime Take on an empty stomach to reduce side effects.	Alternative NRTI for dual-NRTI backbone of combination regimens. TDF would be a preferred NRTI in combination with 3TC or FTC in women with chronic HBV infection. Because of potential for renal toxicity, renal function should be monitored.	AUC lower in third trimester than postpartum but trough levels adequate[14]. High placental transfer.[15-18].	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. Studies in monkeys at doses approximately 2-fold higher than that for human therapeutic use show decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy[19]. Clinical studies in humans (particularly children) show bone demineralization with chronic use; clinical significance unknown[20-21]. Significant placental passage in humans (cord:maternal blood ratio 0.6–0.99). If hepatitis B coinfected, possible hepatitis B flare if drug stopped postpartum, see Special Considerations: Hepatitis B Virus Coinfection.
NNRTIs			NNRTIs are recommended for use in combination regimens with 2 NRTI drugs.		Hypersensitivity reactions, including hepatic toxicity, and rash more common in women; unclear if increased in pregnancy.
Preferred Agents					
Nevirapine (NVP) Viramune	200-mg tablets or 50-mg/5-mL oral suspension	200 mg once daily for 14 days (lead-in period); thereafter, 200 mg BID Take without regard to meals. Repeat lead-in period if therapy is discontinued for >7 days. In patients who develop mild-to-moderate rash without constitutional symptoms during lead-in, continue lead-in dosing until rash resolves, but not >28 days total.	NVP should be initiated in pregnant women with CD4 counts >250 cells/mm^3 only if benefit clearly outweighs risk because of the increased risk of potentially life-threatening hepatotoxicity in women with high CD4 cell counts. Women who enter pregnancy on NVP regimens and are tolerating them well may continue therapy, regardless of CD4 count.	PK not significantly altered in pregnancy; no change in dose indicated [22-24]. High placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 cell counts >250/mm^3 when first initiating therapy[25-26]; unclear if pregnancy increases risk.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 5 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Use in Special Circumstances					
Efavirenz§ (EFV) Sustiva	50-, 200-mg capsules or 600- mg tablets **Atripla** EFV§ 600 mg + FTC 200 mg + TDF 300 mg	600 mg once daily at or before bedtime Take on an empty stomach to reduce side effects. **Atripla** 1 tablet once daily at or before bedtime	Use of EFV should be avoided in the first trimester. Use after the first trimester can be considered if, after consideration of other alternatives, this is the best choice for a specific woman. If EFV is to be continued postpartum, adequate contraception must be assured. Women of childbearing age must be counseled regarding the teratogenic potential of EFV and avoidance of pregnancy while on the drug. Because of the known failure rates of contraceptive methods, alternative ARV regimens should be strongly considered in women of childbearing potential.	AUC decreased during third trimester, compared with postpartum, but nearly all third-trimester subjects exceeded target exposure and no change in dose is indicated[27]. Moderate placental transfer to fetus.	FDA Pregnancy Class D; significant malformations (anencephaly, anophthalmia, cleft palate) were observed in 3 of 20 infants (15%) born to cynomolgus monkeys receiving EFV during the first trimester at a dose resulting in plasma levels comparable to systemic human therapeutic exposure. There are 6 retrospective case reports and 1 prospective case report of neural tube defects in humans with first-trimester exposure and 1 prospective case of anophthalmia with facial clefts[28-30]; relative risk unclear.
Insufficient Data to Recommend Use					
Etravirine (ETR) Intelence	100-, 200-mg tablets	200 mg BID Take following a meal.	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy.	No PK studies in human pregnancy, placental transfer rate unknown.	No experience in human pregnancy.
Rilpivirine (RPV) Endurant	25-mg tablets **Complera** RPV 25 mg + TDF 300 mg + FTC 200 mg	25 mg once daily with a meal. **Complera** 1 tablet once daily	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy.	No PK studies in human pregnancy, placental transfer rate unknown.	No experience in human pregnancy.
PIs			PIs are recommended for use in combination regimens with 2 NRTI drugs.		Hyperglycemia, new onset or exacerbation of diabetes mellitus, and diabetic ketoacidosis reported with PI use; unclear if pregnancy increases risk. Conflicting data regarding preterm delivery in women receiving PIs (see Protease Inhibitor Therapy and Hyperglycemia).

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 6 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Preferred Agents					
Lopinavir + Ritonavir (LPV/r) Kaletra	**Tablets:** (LPV 200 mg + RTV 50 mg) or (LPV 100 mg + RTV 25 mg) **Oral solution:** Each 5 mL contains (LPV 400 mg + RTV 100 mg) Oral solution contains 42% alcohol	LPV/r 400 mg/100 mg BID **Third trimester:** Some experts recommend increased dose LPV/r 600 mg/150 mg BID in third trimester **With EFV or NVP (PI-naive or PI-experienced patients):** LPV/r 500 mg/125 mg tablets BID (use a combination of two LPV/r 200 mg/50 mg tablets + one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg.) or LPV/r 533 mg/133 mg oral solution (6.5 mL) BID **Tablets:** Take without regard to meals. **Oral solution:** Take with food. **Not used in pregnancy:** Adult dosage of LPV/r 800 mg/200 mg once daily is not recommended for use in pregnancy.	PK studies suggest dose should be increased to 600 mg/150 mg BID in second and third trimester, especially in PI-experienced patients. If standard dosing is used, monitor virologic response and LPV drug levels, if available. Once-daily LPV/r dosing is not recommended during pregnancy because there are no data to address whether drug levels are adequate with such administration.	AUC decreased in second and third trimester with standard dosing[31-33]. AUC with dose of LPV/r 600 mg/150 mg twice daily in third trimester in women in the United States resulted in AUC similar to that in nonpregnant adults taking LPV/r 400 mg/100 mg dose twice daily[12]. Low placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. Well-tolerated, short-term safety demonstrated in Phase I/II studies.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 7 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Alternative Agents					
Atazanavir (ATV) Reyataz (combined with low-dose RTV boosting)	100-, 150-, 200-, 300-mg capsules	**ARV-naive patients:** (ATV 300 mg + RTV 100) mg once daily **With TDF or H2-receptor antagonist (not both) in ARV-experienced nonpregnant patients:** (ATV 300 mg + RTV 100 mg) once daily; **in pregnant patients:** (ATV 400 mg + RTV 100 mg) once daily. **With EFV (after first trimester) in ARV-naive patients:** (ATV 400 mg + RTV 100 mg) once daily (For dosing recommendations with H2 antagonists and PPIs in treatment-naive patients, refer to Adult Guidelines.) Take with food.	Alternative PI for use in combination regimens in pregnancy. Should give as low-dose RTV-boosted regimen, may use once daily dosing. A study of 41 pregnant women described in the package insert for Reyataz concluded that no dose adjustment of ATV was needed for the majority of pregnant women infected with strains of HIV susceptible to ATV. The exception was in ART-experienced pregnant women on either tenofovir or H2-receptor blocker (not both) who should receive increase in ATV dose to 400 mg (with ritonavir 100 mg).	Two of three intensive PK studies of ATV with RTV boosting during pregnancy and the PK study described in the recently approved product label suggest that standard dosing results in decreased plasma concentrations, compared with nonpregnant adults[15, 34-36]. However, for most pregnant women (not on interacting concomitant medications), no dose adjustment was needed. ATV concentrations further reduced ~25% with concomitant TDF use[15, 36]. Low placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4]. Transplacental passage is low, with cord blood concentration averaging 10%–19% of the maternal delivery ATV concentration[15, 34, 36]. Theoretical concern regarding increased indirect bilirubin levels causing significant exacerbation in physiologic hyperbilirubinemia in neonates has not been observed in clinical trials to date[15, 34-37].
Ritonavir (RTV) Norvir	100-mg capsules 100-mg tablets 80-mg/mL oral solution Oral solution contains 43% alcohol	**As PK booster for other PIs:** 100–400 mg per day in 1–2 divided doses (refer to other PIs for specific dosing recommendations) **Tablets:** Take with food. **Capsule and oral solution:** Take with food if possible, which may improve tolerability.	Given low levels in pregnant women when used alone, should only be used in combination with second PI as low-dose RTV "boost" to increase levels of second PI.	Phase I/II study in pregnancy showed lower levels during pregnancy compared with postpartum[38]. Minimal placental transfer to fetus.	Limited experience at full dose in human pregnancy; has been used as low-dose RTV boosting with other PIs. No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[4].

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 8 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Saquinavir (SQV) Invirase (Available as hard gelatin capsules and tablets. SQV must be combined with low-dose RTV boosting.)	500-mg tablets or 200-mg hard gelatin capsules	(SQV 1,000 mg + RTV 100 mg) BID Unboosted SQV is **not** recommended. Take with meals or within 2 hours after a meal.	PK data on SQV hard gelatin capsules and the new tablet formulation in pregnancy are limited. RTV-boosted SQV hard gelatin capsules or SQV tablets are alternative PIs for combination regimens in pregnancy and are alternative initial ARV recommendations for nonpregnant adults. Must give as low-dose RTV-boosted regimen.	Limited PK data on SQV hard gelatin capsules and the new 500-mg tablet formulation suggest that 1,000 mg SQV hard gelatin capsules/100 mg RTV given twice daily achieves adequate SQV drug levels in pregnant women[39]. Minimal placental transfer to fetus.	Well-tolerated, short-term safety demonstrated for mothers and infants for SQV in combination with low-dose RTV. Baseline EKG recommended before starting because PR and/or QT interval prolongations have been observed.
Use in Special Circumstances					
Indinavir (IDV) Crixivan (combined with low-dose RTV boosting)	100-, 200-, 400- mg capsules	**With RTV:** (IDV 800 mg + RTV 100– 200 mg) BID Take without regard to meals. **Not used in pregnancy:** Adult dosage of IDV (without RTV) 800 mg every 8 hours is not recommended for use in pregnancy.	Because of twice-daily dosing, pill burden, and potential for renal stones, IDV should only be used when preferred and alternative agents cannot be used. Must give as low-dose RTV-boosted regimen.	Two studies including 18 women receiving IDV 800 mg three times daily showed markedly lower levels during pregnancy compared with postpartum, although suppression of HIV RNA levels was seen[40-41]. In a study of RTV-boosted IDV (400 mg IDV/100 mg RTV twice daily), 82% of women met the target trough level[42]. Minimal placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[28]. Theoretical concern regarding increased indirect bilirubin levels, which may exacerbate physiologic hyperbilirubinemia in neonates, but minimal placental passage. Use of unboosted IDV during pregnancy is not recommended.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 9 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Nelfinavir (NFV) Viracept	250-, 625-mg tablets 50-mg/g oral powder	1,250 mg BID Take with food. **Not used in pregnancy:** Adult dosage of NFV 750 mg TID is not recommended for use in pregnancy.	Given PK data and extensive experience with use in pregnancy, NFV might be considered in special circumstances for prophylaxis of transmission in women in whom therapy would not otherwise be indicated when alternative agents are not tolerated. In clinical trials of initial therapy in non-pregnant adults, NFV-based regimens had a lower rate of viral response compared with LPV/r or EFV-based regimens, but similar viral response to ATVor NVP-based regimens.	Adequate drug levels are achieved in pregnant wome with NFV 1,250 mg given twice daily, although levels are variable in late pregnancy[23, 43-44]. In a study of pregnant women in their second and third trimester dosed at 1,250 mg given twice daily, women in the third trimester had lower concentration of NFV than women in the second trimester[44]. In a study of the new 625-mg tablet formulation dosed at 1,250 mg twice daily, lower AUC and peak levels were observed during the third trimester of pregnancy than postpartum[45]. Minimal to low placental transfer to fetus.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects)[28]. Well-tolerated, short-term safety demonstrated for mothers and infants.
Insufficient Data to Recommend Use					
Darunavir (DRV) Prezista (must be combined with low-dose RTV boosting)	75-, 150-, 400-, 600-mg tablets	**ARV-naive patients:** (DRV 800 mg + RTV 100 mg) once daily **ARV-experienced patients:** (DRV 800 mg + RTV 100 mg) once daily if no DRV resistance mutations (DRV 600 mg + RTV 100 mg) BID if any DRV resistance mutations Unboosted DRV is **not** recommended. Take with food.	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy in ARV-naive patients. Must give as low-dose RTV-boosted regimen.	No PK studies in human pregnancy. Minimal to low placental transfer to fetus[46].	No experience in human pregnancy.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 10 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Fosamprenavir (FPV) Lexiva (a prodrug of amprenavir) (recommended to be combined with low-dose RTV boosting)	700-mg tablet or 50-mg/mL oral suspension	**ARV-naive patients:** • FPV 1,400 mg BID or • (FPV 1,400 mg + RTV 100–200 mg) once daily or • (FPV 700 mg + RTV 100 mg) BID **PI-experienced patients (once-daily dosing not recommended):** • (FPV 700 mg + RTV 100 mg) BID **With EFV:** • (FPV 700 mg + RTV 100 mg) BID or • (FPV 1,400 mg + RTV 300 mg) once daily **Tablet:** Take without regard to meals (if not boosted with RTV tablet). **Suspension:** Take without food. **FPV with RTV tablet:** Take with meals.	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy in ARV-naive patients. Recommended to be given as low-dose RTV-boosted regimen.	With RTV boosting, AUC is reduced during the third trimester. However, exposure is greater during the third trimester with boosting than in nonpregnant adults without boosting and trough concentrations achieved during the third trimester were adequate for patients without PI resistance mutations[47]. Low placental transfer to fetus.	Limited experience in human pregnancy.
Tipranavir (TPV) Aptivus (must be combined with low-dose RTV boosting)	250-mg capsules or 100-mg/mL oral solution	(TPV 500 mg + RTV 200 mg) BID Unboosted TPV is **not** recommended. **TPV taken with RTV tablets:** Take with meals. **TPV taken with RTV capsules or solution:** Take without regard to meals.	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy in ARV-naive patients. Must give as low-dose RTV-boosted regimen.	No PK studies in human pregnancy. Unknown rate of placental transfer to fetus.	No experience in human pregnancy.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (Page 11 of 11)

ARV Drug Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations*	Recommendations for Use in Pregnancy	PKs in Pregnancy†	Concerns in Pregnancy
Entry Inhibitors					
Insufficient Data to Recommend Use					
Enfuvirtide (T20) Fuzeon	• Injectable— supplied as lyophilized powder • Each vial contains 108 mg of T20; reconstitute with 1.1 mL of sterile water for injection for delivery of approximately 90 mg/1 mL	90 mg (1mL) SQ BID	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy in ARV-naive patients.	No PK studies in human pregnancy. No placental transfer to fetus, based on very limited data.	Minimal data in human pregnancy[48].
Maraviroc (MVC) Selzentry	150-, 300-mg tablets	• 150 mg BID when given with strong CYP3A inhibitors (with or without CYP3A inducers) including PIs (except TPV/r) • 300 mg BID when given with NRTIs, T-20, TPV/r, NVP, and other drugs that are not strong CYP3A inhibitors or inducers • 600 mg BID when given with CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take without regard to meals.	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy in ARV-naive patients.	No PK studies in human pregnancy. Unknown placental transfer rate to fetus.	No experience in human pregnancy
Integrase Inhibitors					
Insufficient Data to Recommend Use					
Raltegravir (RAL) Isentress	400-mg tablets	400 mg BID With rifampin: 800 mg BID Take without regard to meals.	Safety and PK data in pregnancy are insufficient to recommend use during pregnancy.	During third trimester, RAL PK show extensive variability but RAL exposure was not consistently altered, compared with postpartum and historical data. The standard dose appears appropriate during pregnancy[49]. Variable but high placental transfer to fetus.	No experience in human pregnancy.

Key to Abbreviations: ARV = antiretroviral; AUC = area under the curve; BID = twice daily; CYP = cytochrome P; EKG = electrocardiogram; FDA = Food and Drug Administration; IV = intravenous; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside/nucleotide reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; SQ = subcutaneous injection; TID = three times daily; WHO = World Health Organization

* Dosage should be adjusted in renal or hepatic insufficiency (see Adult Guidelines, Appendix B, Table 7).

‡ Triple-NRTI regimens including abacavir have been less potent virologically compared with PI-based combination ARV drug regimens. Triple-NRTI regimens should be used only when an NNRTI- or PI-based combination regimen cannot be used, such as because of significant drug interactions.

§ See section on Teratogenicity for discussion of efavirenz and risks in pregnancy.

† Placental transfer categories—Mean or median cord blood/maternal delivery plasma drug ratio:
High: >0.6
Moderate: 0.3–0.6
Low: 0.1–0.3
Minimal: <0.1

ARV drugs for prevention of perinatal transmission of HIV are recommended for all pregnant women, regardless of whether they have indications for ART for their own health. In general, guidelines for the use of ART for the benefit of maternal health during pregnancy are the same as for women who are not pregnant, with some modifications, based on concerns about specific drugs and limited experience during pregnancy with newer drugs. ARV prophylaxis is recommended for all pregnant women with HIV infection who do not require therapy, regardless of viral load (see HIV-Infected Pregnant Women Not on Antiretroviral Therapy Who Require Antiretroviral Prophylaxis Solely to Prevent Perinatal Transmission of HIV).

Decisions regarding initiation or modification of ARV drug regimens during pregnancy include considerations regarding the benefits and risks of ARV drug use that are common to all HIV-infected adults in addition to considerations unique to pregnancy. In general, the ARV drug combinations now available are more convenient and better tolerated than regimens used previously, resulting in greater efficacy and improved adherence. During pregnancy maternal ARV toxicities must be considered, along with the potential impact of the ARV regimen on pregnancy outcome and on the fetuses and infants. Decisions about ARV drug regimens are further complicated because only limited data exist on the long-term maternal consequences of use of the agents during pregnancy solely for prophylaxis of transmission. Similarly, only limited data are available on the long-term consequences to infants of *in utero* exposure to ARVs.

The known benefits and known and unknown risks of ARV drug use during pregnancy should be considered and discussed with women (see Special Considerations Regarding the Use of Antiretroviral Drugs by HIV-infected Pregnant Women and their Infants). Results from preclinical and animal studies and available clinical information about use of the various agents during pregnancy also should be discussed (see Supplement: Safety and Toxicity of Individual Antireroviral Agents in Pregnancy). Potential risks of these drugs should be placed into perspective by reviewing the substantial benefits of ARV drugs for maternal health and in reducing the risk of transmission of HIV to infants. Counseling of pregnant women about ARV use should be noncoercive, and providers should help women make informed decisions regarding use of ARV drugs.

Discussions with women about initiation of ARV drug regimens should include information about:

a. maternal risk of disease progression and the benefits and risks of initiation of therapy for maternal

health;

b. benefit of combination ARV regimens for preventing perinatal transmission of HIV[50];

c. potential adverse effects of ARV drugs for mothers, fetuses, and infants, including potential interactions with other medications the women may already be receiving;

d. the limited long-term outcome data for both women who temporarily use ARV drugs during pregnancy for prophylaxis of transmission and infants who are exposed to ARVs *in utero*; and

e. the possibility of development of ARV resistance, including the need for strict adherence to the prescribed drug regimen to avoid it.

Studies of zidovudine for the prevention of perinatal transmission suggest that pre-exposure prophylaxis of the infant from transplacental passage of drug is an important component of prevention. Thus, when selecting an ARV regimen for a pregnant woman, at least one nucleoside/nucleotide (NRTI) agent with high placental transfer should be included as a component of the dual NRTI backbone (see Table 5)[13, 18, 51-52].

In women with plasma HIV RNA above the threshold for resistance testing (e.g., >500–1,000 copies/mL), ARV drug-resistance studies should be performed before starting ARV drugs for maternal health or prophylaxis. When HIV is diagnosed late in pregnancy, however, ARV drugs should be initiated pending results of resistance testing (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy).

Counseling should emphasize the importance of adherence to the ARV drug regimen. Support services, mental health services, and drug abuse treatment may be required, depending on women's individual circumstances. Coordination of services among prenatal care providers, primary care and HIV specialty care providers, mental health and drug abuse treatment services, and public assistance programs is essential to ensure that infected women adhere to their ARV drug regimens.

Providers should work with women to develop long-range plans regarding continuity of medical care and decisions about treatment for their own health after giving birth. Considerations regarding continuation of the ARV regimen for maternal therapeutic indications are the same following delivery as for nonpregnant individuals. The impact on short- and long-term maternal health is unknown for postpartum discontinuation of combination ARV drug regimens used solely to prevent perinatal transmission. This is particularly important because women may have multiple pregnancies resulting in episodic receipt of ARV drugs. No increase in disease progression has been seen so far, however, in studies of pregnant women with relatively high CD4 counts who stop combination ARV drug regimens after delivery[53-55]. The risks versus benefits of stopping ARV drug regimens postpartum in women with high CD4 cell counts are being evaluated in the ongoing PROMISE study (clinical trial number NCT00955968).

Current adult treatment guidelines strongly recommend ART for all individuals with CD4 cell counts <350 cells/mm^3 based on randomized, controlled clinical trial data demonstrating a clear benefit in reduction of mortality and morbidity. Pregnant women with CD4 counts <350 cells/mm^3 should begin on combination ART as soon as possible during pregnancy and be counseled about the need to continue therapy after delivery and the importance of adherence to the regimen.

Based on observational cohort data, the adult treatment guidelines make a moderate-to-strong recommendation for initiating lifelong ART in individuals with CD4 cell counts between 350 and 500 cells/mm^3. Observational studies suggest a relative decrease in mortality (although the overall number of events was small) and possibly a decrease in complications such as cardiovascular events with initiation of ART in this setting compared with waiting until CD4 cell counts drop below 350 cells/mm^3 [56-57]. Preg-

nant women with CD4 cell counts between 350 and 500 cells/mm^3 should be started on a combination ARV regimen during pregnancy to prevent perinatal transmission of HIV and counseled about the current treatment recommendations, the potential risks versus benefits of stopping versus continuing the regimen after delivery, and the need for strict adherence if the regimen is continued postpartum.

For individuals with CD4 counts >500 cells/mm^3, the adult guidelines note that some experts would recommend initiating lifelong therapy, while other experts would view this as optional, given that data are inconclusive on the clinical benefit of starting treatment at higher CD4 cell counts (>500 cells/mm^3). So far, no increased risk of disease progression has been shown in studies of pregnant women with relatively high CD4 counts who stop ARV drugs after delivery[53-55]. The potential benefits of early therapy must be weighed against possible drug toxicity, cost, and the risk of development of viral resistance with suboptimal adherence, which may be more likely during the postpartum period[58]. Pregnant women with CD4 cell counts >500 cells/mm^3 should be started on a combination ARV regimen during pregnancy to prevent perinatal transmission. They should be assessed for their willingness and ability to commit to ongoing continuous therapy and counseled about the current treatment guidelines, the benefits and risks of therapy, that data on the clinical benefit of starting lifelong treatment at CD4 cell counts >500 cells/mm^3 are inconclusive, and the importance of adherence if the regimen is continued postpartum.

In general, when drugs are discontinued postnatally, all drugs should be stopped simultaneously. However, as discussed later (see Stopping Antiretroviral Therapy during Pregnancy), in women receiving non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens, continuing the dual-NRTI backbone for a period of time after stopping the NNRTI is recommended to reduce the development of NNRTI resistance. An alternative strategy is to replace the NNRTI with a protease inhibitor (PI) drug while continuing the NRTI, then to discontinue all the drugs at the same time[59]. The optimal interval between stopping an NNRTI and stopping the other ARV drugs is unknown, but a minimum of 7 days is recommended. Drug concentrations may be detectable for more than 3 weeks after efavirenz is stopped in patients receiving an efavirenz-based NNRTI regimen. Therefore, for patients receiving efavirenz, some experts recommend continuing the other ARV agents or substituting a PI plus two other agents for up to 30 days.

Medical care of HIV-infected pregnant women requires coordination and communication between HIV specialists and obstetrical providers. General counseling should include current knowledge about risk factors for perinatal transmission. Risk of perinatal transmission of HIV has been associated with potentially modifiable factors including cigarette smoking, illicit drug use, genital tract infections, and unprotected sexual intercourse with multiple partners during pregnancy[60-64]. Besides improving maternal health, cessation of cigarette smoking and drug use, treatment of genital tract infections, and use of condoms with sexual intercourse during pregnancy may reduce risk of perinatal transmission. In addition, the Centers for Disease Control and Prevention (CDC) recommends that HIV-infected women in the United States (including those receiving ART) refrain from breastfeeding to avoid postnatal transmission of HIV to their infants through breast milk[65].

The National Perinatal HIV Hotline (1-888-448-8765)

The National Perinatal HIV Hotline is a federally funded service providing free clinical consultation to providers caring for HIV-infected women and their infants.

Recommendations for Use of Antiretroviral Drugs During Pregnancy

The Panel recommends that choice of ARV drug regimens for HIV-infected pregnant women be based on the same principles used to choose regimens for nonpregnant individuals, unless there are compelling

pregnancy-specific maternal or fetal safety issues associated with specific drugs. The Panel reviews clinical trial data published in peer-reviewed journals and data prepared by manufacturers for Food and Drug Administration (FDA) review related to treatment of HIV-infected adult women, both pregnant and nonpregnant. The durability, tolerability, and simplicity of a medication regimen is particularly important for preserving future options for women who will be stopping medications after delivery and women who meet standard criteria for initiation of ART per adult guidelines and will continue the regimen after pregnancy. Regimen selection should be individualized and the following factors should be considered:

- comorbidities;
- patient adherence potential;
- convenience;
- potential adverse maternal drug effects;
- potential drug interactions with other medications;
- results of genotypic resistance testing;
- pharmacokinetic (PK) changes in pregnancy; and
- potential teratogenic effects and other adverse effects on fetuses or newborns.

Information used by the Panel for recommending specific drugs or regimens for pregnant women include:

- Data from randomized prospective clinical trials that demonstrate durable viral suppression as well as immunologic and clinical improvement;
- Incidence rates and descriptions of short- and long-term drug toxicity of ARV regimens, with special attention to maternal toxicity and potential teratogenicity and fetal safety;
- Specific knowledge about drug tolerability and simplified dosing regimens;
- Known efficacy of some drug regimens in reducing mother-to-child transmission of HIV;
- PK data during the prenatal period. (The physiologic changes of pregnancy have the potential to alter drug PKs. ARV dosing during pregnancy should be based on PK data from studies in pregnant women. Physiologic changes are not fixed throughout pregnancy but, rather, reflect a continuum of change as pregnancy progresses, with return to baseline at various rates in the postpartum period.); and
- Data from animal teratogenicity studies.

Categories of ARV regimens include:

- **Preferred:** Drugs or drug combinations are designated as preferred for use in pregnant women when clinical trial data in adults have demonstrated optimal efficacy and durability with acceptable toxicity and ease of use; pregnancy-specific PK data are available to guide dosing; and no evidence of teratogenic effects or established association with teratogenic or clinically significant adverse outcomes for mothers, fetuses, or newborn are present.
- **Alternative:** Drugs or drug combinations are designated as alternatives for initial therapy in pregnant women when clinical trial data in adults show efficacy but any one or more of the following conditions apply: experience in pregnancy is limited; data are lacking on teratogenic effects on the fetus; or the drug or regimen is associated with dosing, formulation, administration, or interaction issues.

- **Use in Special Circumstances:** Drug or drug combinations in this category can be considered for use when intolerance or resistance prohibits use of other drugs with fewer toxicity concerns or in women who have comorbidities or require concomitant medications that may limit drug choice, such as active tuberculosis requiring rifampin therapy.
- **Not Recommended:** Drugs and drug combinations listed in this category are not recommended for therapy in pregnant women because of inferior virologic response, potentially serious maternal or fetal safety concerns, or pharmacologic antagonism.
- **Insufficient Data to Recommend:** The drugs and drug combinations in this category are approved for use in adults but lack pregnancy-specific PK or safety data, or such data are too limited to make a recommendation for use for pregnancy.

A combination ARV regimen with at least three agents is recommended for use in pregnancy for either treatment or prophylaxis. Recommendations for choice of ARV drug regimen during pregnancy must be individualized according to a pregnant woman's specific ARV history and the presence of comorbidities. Some women may become pregnant and present for obstetrical care while receiving ART for their own health. In these cases, the choice of active drugs with known safety data in pregnancy may be more limited. In general, women who are already on a fully suppressive regimen should continue their regimens. Use of efavirenz, however, should be avoided in the first trimester.

Other HIV-infected women may not be receiving ART at the time they present for obstetrical care. Some women have never received ARV drugs, while others may have taken ARV drugs for treatment that was stopped or for prophylaxis to prevent perinatal transmission of HIV in prior pregnancies or for pre- or post-exposure prophylaxis. Considerations for initiating therapy in pregnant women differ, depending upon whether ARV drugs are currently indicated for maternal health or solely for fetal protection. The following sections will provide detailed discussions of recommendations based on maternal ARV history and whether there are maternal indications for therapy.

For ARV-naive women, a combination regimen including two NRTIs and either an NNRTI or a PI (generally with low-dose ritonavir) would be preferred.

The preferred NRTI combination for ARV-naive pregnant women is zidovudine/lamivudine, based on efficacy studies in preventing perinatal transmission (see Lessons from Clinical Trials of Antiretroviral Interventions to Reduce Perinatal HIV Transmission) and large experience with safety of use in pregnancy. Alternate regimens can be used in women who are intolerant of zidovudine because of toxicity such as severe anemia or who have known resistance to the drug.

Tenofovir is a preferred NRTI for nonpregnant women. Data from the Antiretroviral Pregnancy Registry on 1,092 pregnancies with first-trimester exposure to tenofovir have shown no increase in overall birth defects compared with the general population[4]. Animal studies, however, have shown decreased fetal growth and reduction in fetal bone porosity, and studies in infected children on chronic tenofovir-based therapy have shown bone demineralization in some children. Therefore, tenofovir would be considered an alternative NRTI during pregnancy for ARV-naive women. For pregnant women with chronic hepatitis B infection, however, tenofovir in combination with emtricitabine or lamivudine would be the preferred NRTI backbone of a combination ARV regimen. The combination of stavudine/didanosine should not be used in pregnant women because fatal cases of lactic acidosis and hepatic failure have been reported in women who received this combination throughout pregnancy.

In addition to the two NRTIs, either an NNRTI or a PI would be preferred for combination regimens in ARV-naive pregnant women. Efavirenz, the preferred NNRTI for nonpregnant adults, is not recom-

mended for use in the first trimester because non-human primate data show risk of anencephaly, microophthalmia, and cleft palate, and there are several concerning case reports of neural tube defects and a single case of anophthalmia with severe facial cleft in humans. Use of efavirenz can be considered after the first trimester, based on clinical indication, but current data are limited in defining the safety of this use. Nevirapine would be the preferred NNRTI for ARV-naive pregnant women with CD4 cell lymphocyte counts <250 cells/mm^3, and it can be continued in ARV-experienced women already receiving a nevirapine-based regimen, regardless of CD4 cell count. In general, nevirapine should not be initiated in treatment-naive women with CD4 cell counts >250 cells/mm^3 because of an increased risk of symptomatic and potentially fatal rash and hepatic toxicity (see Special Considerations Regarding the Use of Antiretroviral Drugs by HIV-Infected Pregnant Women and their Infants). Elevated transaminase levels at baseline also may increase the risk of nevirapine toxicity[66]. Safety and PK data on etravirine and rilpivirine in pregnancy are insufficient to recommend use of these NNRTI drugs in ARV-naive women.

Lopinavir/ritonavir is the preferred PI regimen for ARV-naive pregnant women, based on efficacy studies in adults and experience with use in pregnancy (see Table 5 for dosing considerations). Alternative PIs include ritonavir-boosted atazanavir or saquinavir, although experience is more limited with these regimens in pregnancy. Nelfinavir can be considered in special circumstances when used solely for prophylaxis of perinatal transmission in ARV-naive women for whom therapy would not otherwise be indicated and who cannot tolerate alternative agents. PK data and extensive clinical experience do exist for nelfinavir in pregnancy, but the rate of viral response to nelfinavir-based regimens was lower than lopinavir/ritonavir or efavirenz-based regimens in clinical trials of initial therapy in nonpregnant adults. Indinavir can also be considered in special circumstances for women in whom preferred or alternative drugs cannot be used. Indinavir may be associated with renal stones and has a higher pill burden than many other PI drugs. Data on use in pregnancy are too limited to recommend routine use of darunavir, fosamprenavir, and tipranavir in pregnant women, although they can be considered for women who are intolerant of other agents.

Safety and PK data in pregnancy are insufficient to recommend use of the entry inhibitors enfuvirtide and maraviroc and the integrase inhibitor raltegravir during pregnancy. Use of these agents can be considered for women who have failed therapy with several other classes of ARV drugs after consultation with HIV and obstetric specialists.

Although data are insufficient to support or refute the teratogenic risk of ARV drugs when administered during the first trimester, information to date does not support major teratogenic effects for the majority of such agents. (For further data, see http://www.APRegistry.com.) However, certain drugs are of more concern than others—for example, efavirenz should be avoided during the first trimester of pregnancy (see Supplement: Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy).

Table 5 provides recommendations for use of specific ARV drugs in pregnancy and data on PKs and toxicity in pregnancy. Table 6 summarizes management recommendations for the mothers and infants in a variety of clinical scenarios.

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States (Page 1 of 4)

Clinical Scenario	Recommendations
Nonpregnant HIV-infected women of childbearing potential who have indications for initiating antiretroviral therapy (ART)	Initiate combination antiretroviral (ARV) drug therapy as per adult treatment guidelines. When feasible, include one or more nucleoside reverse transcriptase inhibitors (NRTIs) with good placental passage as a component of the ARV regimen. • Avoid drugs with teratogenic potential (e.g., efavirenz) in women who are trying to conceive or are not using adequate contraception. Exclude pregnancy and ensure access to effective contraception before starting treatment with efavirenz.
HIV-infected women on combination ARV drug therapy who become pregnant	**Women:** • In general, in women who require treatment, ARV drugs should not be stopped during the first trimester or during pregnancy. • Continue current combination ART, if successfully suppressing viremia; however, avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (e.g., combination stavudine/didanosine) throughout the pregnancy. • Perform HIV ARV drug-resistance testing in women on therapy who have detectable viremia. • Continue combination ART regimen during the intrapartum period (zidovudine given as continuous infusion[a] during labor while other ARV agents are continued orally) and postpartum. • Schedule cesarean delivery at 38 weeks of gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infants:** • Start zidovudine as soon as possible after birth and administer for 6 weeks.[b]

HIV-infected pregnant women who are ARV naive *and* have indications for ART	**Women:**
	• Perform HIV ARV drug-resistance testing prior to initiating combination ARV drug therapy and repeat after initiating therapy if viral suppression is suboptimal.
	• Initiate combination ARV regimen.
	  • Avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (e.g., combination stavudine/didanosine) throughout the pregnancy.
	  • When feasible, include one or more NRTIs with good placental passage in the ARV regimen.
	  • Use nevirapine as a component of the ARV regimen only in women who have CD4 counts ≤250 cells/mm^3. Because of the increased risk of severe hepatic toxicity, use nevirapine in women with CD4 counts >250 cells/mm^3 only if the benefit clearly outweighs the risk.
	• In women who require initiation of therapy for their own health, initiate treatment as soon as possible, including in the first trimester.
	• Continue the combination regimen during the intrapartum period (zidovudine given as continuous infusion[a] during labor while other ARV agents are continued orally) and postpartum.
	• Schedule cesarean delivery at 38 weeks of gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery.
	Infants:
	• Start zidovudine as soon as possible after birth and administer for 6 weeks.[b]

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States (Page 2 of 4)

Clinical Scenario	Recommendations

HIV-infected pregnant women who are ARV naive and do *not* require treatment for their own health	**Women:**
	• Perform HIV ARV drug-resistance testing prior to initiating combination ARV drug therapy and repeat after initiation of therapy if viral suppression is suboptimal.
	• Prescribe combination ARV drug prophylaxis (i.e., at least 3 drugs) to prevent perinatal transmission.
	  • Delayed initiation of prophylaxis until after the first trimester of pregnancy can be considered in women who are receiving ARV drugs solely for prevention of perinatal transmission, but earlier initiation of prophylaxis may be more effective in reducing perinatal transmission of HIV.
	  • Avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (e.g., combination stavudine/didanosine) throughout the pregnancy.
	  • When feasible, use one or more NRTIs with good transplacental passage as a component of the ARV regimen.
	  • Use nevirapine as a component of therapy in women who have CD4 counts >250 cells/mm^3 only if the benefit clearly outweighs the risk because of the drug's association with an increased risk of severe hepatic toxicity.
	• Continue ARV prophylaxis regimen during the intrapartum period (zidovudine given as continuous infusion[a] during labor while other ARV agents are continued orally).
	• Evaluate need for continuing the combination regimen postpartum. Following delivery, considerations for continuation of the mother's ARV regimen are the same as for other nonpregnant individuals (see General Principles Regarding Use of Antiretroviral Drugs in Pregnancy). If treatment is to be stopped and the regimen includes a drug with a long half-life, such as a non-nucleoside reverse transcriptase inhibitor (NNRTI), consider stopping NRTIs at least 7 days after stopping NNRTI. (See Stopping Antiretroviral Therapy Drugs During Pregnancy and Prevention of Antiretroviral Drug Resistance.)
	• Schedule cesarean delivery at 38 weeks of gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery.
	Infants:
	• Start zidovudine as soon as possible after birth and administer for 6 weeks.[b]

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States (Page 3 of 4)

Clinical Scenario	Recommendations

HIV-infected pregnant women who are ARV experienced but not currently receiving ARV drugs	**Women:**
	• Obtain full ARV drug history, including prior resistance testing, and evaluate need for ART for maternal health.
	• Test for HIV ARV drug resistance before re-initiating ARV prophylaxis or therapy and retest after initiating combination ARV regimen if viral suppression is suboptimal.
	• Initiate a combination ARV regimen (e.g., at least 3 drugs), with regimen chosen based on results of resistance testing and history of prior therapy.
	  • In women who require initiation of therapy for their own health, initiate treatment as soon as possible, including in the first trimester.
	  • Delayed initiation of prophylaxis until after the first trimester of pregnancy can be considered in women who are receiving ARV drugs solely for prevention of perinatal transmission, but earlier initiation of prophylaxis may be more effective in reducing perinatal transmission of HIV.
	  • Avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for the mother (e.g., combination stavudine/didanosine) throughout the pregnancy.
	  • When feasible, include one or more NRTIs with good transplacental passage as a component of the ARV regimen.
	  • Use nevirapine as a component of therapy in women who have CD4 counts >250 cells/mm^3 only if the benefit clearly outweighs the risk because of the drug's association with an increased risk of severe hepatic toxicity.
	• Continue the combination regimen during intrapartum period (zidovudine given as continuous infusion[a] during labor while other ARV agents are continued orally).
	• Evaluate need for continuing the combination regimen postpartum. Following delivery, considerations for continuation of the mother's ARV regimen are the same as for other nonpregnant adults (see General Principles Regarding Use of Antiretroviral Drugs in Pregnancy). If treatment is to be stopped and the regimen includes a drug with a long half-life, such as NNRTIs, consider stopping NRTIs at least 7 days after stopping NNRTIs. (See Stopping Antiretroviral Therapy and Prevention of Antiretroviral Drug Resistance.)
	• Schedule cesarean delivery at 38 weeks of gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery.
	Infants:
	• Start zidovudine as soon as possible after birth and administer for 6 weeks.[b]

HIV-infected women who have received no ART before labor	**Women:** Give zidovudine as continuous infusion[1] during labor. **Infants:** Infants born to HIV-infected women who have not received antepartum ARV drugs should receive prophylaxis with a combination ARV drug regimen started as close to the time of birth as possible. Zidovudine[b] given for 6 weeks combined with 3 doses of nevirapine in the first week of life (at birth, 48 hours later, and 96 hours after the second dose) has been shown to be effective in a randomized controlled trial and less toxic than a 3-drug regimen with nelfinavir and lamivudine for 2 weeks and 6 weeks of zidovudine. The 2-drug regimen is preferred due to lower toxicity and because nelfinavir powder is no longer available in the United States (see Infant Antiretroviral Prophylaxis and Table 9). • Evaluate need for initiation of maternal therapy postpartum.

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States (Page 4 of 4)

Clinical Scenario	Recommendations
Infants born to HIV-infected women who have received no ART before or during labor	• Infants born to HIV-infected women who have not received antepartum ARV drugs should receive prophylaxis with a combination ARV drug regimen started as close to the time of birth as possible. Zidovudine[b] given for 6 weeks combined with 3 doses of nevirapine in the first week of life (at birth, 48 hours later, and 96 hours after the second dose) has been shown to be effective in a randomized controlled trial and less toxic than a 3-drug regimen with nelfinavir and laminvudine for 2 weeks and 6 weeks of zidovudine. The 2-drug regimen is preferred due to lower toxicity and because nelfinavir powder is no longer available in the United States (see Infant Antiretroviral Prophylaxis and Table 9). • Evaluate need for initiation of maternal therapy postpartum.

[a] Zidovudine continuous infusion: 2 mg/kg zidovudine intravenously over 1 hour, followed by continuous infusion of 1 mg/kg/hour until delivery.

[b] Zidovudine dosing for infants ≥35 weeks' gestation at birth is 4 mg/kg/dose orally twice daily; for infants <35 weeks of gestation at birth is 1.5 mg/kg/dose intravenously or 2.0 mg/kg/dose orally, every 12 hours, advancing to every 8 hours at 2 weeks of age if ≥30 weeks of gestation at birth or at 4 weeks of age if <30 weeks' gestation at birth.

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